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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF RESEARCH AND DEVELOPMENT
ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
CINCINNATI, OHIO 45268

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Subject: Toxicity Values for the American Chemical Services NPL Site/ Griffin, Indiana

From: Pei-Fung Hurst
Coordinator
Superfund Health Risk Technology Support Center
Chemical Mixtures Assessment Branch

To: Robert Swale
U.S. EPA
Region V

Thru: W. Bruce Peirano
Acting Chief
Chemical Mixtures Assessment Branch

This memo is in response to a request from your contractor, Kevin Domack of Warzyn Engineering, regarding oral reference doses (RfDs) and oral carcinogenicity slope factors for the list of chemicals provided by him. In the information that follows, not available indicates that criteria were not derived in a U.S. EPA document. Minimal Risk Levels (MRLs) proposed by the Agency for Toxic Substances and Disease Registry (ATSDR) are presented when no U.S. EPA values are available.

Information on how to estimate risk associated with exposure to high concentrations of carcinogens is provided in the Risk Assessment Guidance for Superfund (RAGS). A One-Hit Equation is presented on page 8-11 of RAGS for dealing with high risk levels.

Please do not hesitate to contact me at FTS 684-7300 (513-569-7300) if I can be of further assistance.

Attachment

cc: C. DeRosa (ECAO-Cin)
K. Domack (Warzyn Engineering)
B. Means (OS-230)
T. O'Bryan (OS-230)
P. VanLeeuwen (Region V)

Toxicity Values for Chemicals at the American Chemical Services NPL Site

A. ORAL REFERENCE DOSES

Benzene. Not available.

Bis(2-chloroethyl)ether. Not available.

Chloroethane. Not available.

DDD and DDE. Not available.

Dibenzofuran. An oral RfD is currently being developed by this Technical Support Center and is expocted to be available around the middle of December.

1,3-Dichlorobenzene. An oral RfD was not derived in the Health Effects Assessment for Dichlorobenzenes (U.S. EPA, 1987a) due to the lack of adequate data. An interim oral RfD of 89 ug/kg/day has been derived in a Drinking Water Health Advisory (U.S. EPA, 1987b).

U.S. EPA. 1987a. Health Effects Assessment for Dichlorobenzenes. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, Ohio, for the Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 1987b. Drinking Water Health Advisory for Ortho-, Meta-, and Para-Dichlorobenzenes. Office of Drinking Water, Washington, DC.

1,2-Dichloroethane. Not available.

1,2-Dichloropropane. Not available. A chronic oral MRL of 0.09 mg/kg/day was derived by ATSDR (ATSDR, 1989)

ATSDR. 1989. Toxicological Profile for 1,2-Dichloropropane. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Final Draft.

2,4-Dinitrotoluene

No EPA documentation could be located for this compound. An external literature search was preformed and adequate data was obtained to derive an interim oral RfD.

Three studies were located that examined the toxic effects of 2,4-dinitrotoluene following subchronic and chronic oral exposure in rats, dogs and mice.

In a 13-week study, CD rats (16/sex/group) were fed a diet containing 0, 34, 93, 266 mg/kg/day (male) or 0, 38, 108, 145 mg/kg/day (female) 2,4-dinitrotoluene (Lee et al., 1985). Increased mortality (6/8 male, 8/8 female) was observed in the high dose groups. Decreased body weight gain was observed in the rats treated at the low dose. Reticulocytosis, splenic hemosiderosis, and demyelination of the cerebellum and brain stem were observed in animals in the middle dose group. In another study conducted by Lee et al. (1985), rats (38/sex/group) were fed for 2 years a diet containing 2,4-dinitrotoluene 0, 0.57, 3.0, 34 mg/kg/day (male) or 0, 0.71, 5.1, 45 mg/kg/day (female). A progression from mild heptacellular lesions to neoplastic nodules or carcinoma was noted to occur in a dose-related manner in male rats. Heptacellular lesions were observed in male rats in the low-, mid- and high-dose groups at incidences of 7/8, 6/8 and 5/7, respectively, while neoplastic nodules were located in 1/8, 0/8 and 6/7 animals, respectively. In female rats receiving the high-dose, neoplastic nodules were noted in 7/8 animals, and one animal had a heptacellular carcinoma. An increased incidence of hepatocellular carcinoma, excessive spleen pigmentation and atrophy of the seminiferous tubules were observed in the high dose group.

Beagle dogs were administered 2,4-dinitrotoluene via a capsule for 13 weeks (n=4/sex/group) or 2 years (n=6/sex/group) (Ellis et al., 1985). The dogs were administered 0, 1, 5, 25 mg/kg/day in the 13-week study and 0, 0.2, 1.5, 10 mg/kg/day in the 2-year study. Incoordination, stiffness, hind leg paralysis and total paralysis were observed in the dogs treated with 25 mg/kg/day for 13 weeks or 10 mg/kg/day for 2 years. Neurotoxic effects were also observed in 1 dog administered 1.5 mg/kg/day; this incidence (1/12) is not significantly different from the control group (0/12). Compensated anemia was observed in the dogs treated for 2 years with 10 mg/kg/day 2,4-dinitrotoluene. Degeneration of the testis and decreased spermatogenesis were observed in dogs administered 25 mg/kg/day for 13 weeks.

CD-1 mice were fed a diet containing 0, 47, 137, 413 mg/kg/day (male) or 0, 52, 147, 468 mg/kg/day (female) for 13 weeks or 0, 14, 95, 898 mg/kg/day (male and female) for 2 years (Hong et al., 1985). In the 13-week study, increased mortality, anemia, testicular degeneration and hepatocellular dysplasia were observed in the high dose animals. Hepatocellular dysplasia and renal tumors were observed in the male mice treated with 2,4-dinitrotoluene for 2 years. Hepatocellular dysplasia was also observed in the female mice treated with 898 mg/kg/day for 2 years. Testicular atrophy and decreased spermatogenesis were observed in the mice exposed to 95 mg/kg/day or greater for 2 years.

The oral RfD for 2,4-dinitrotoluene was based on the dog NOAEL of 0.2 mg/kg/day. Although neurotoxic effects were observed in only one dog receiving 1.5 mg/kg/day, this endpoint was a dose-related effect of exposure to 2,4-dinitrotoluene, occurring with greater frequency in the high-dose group. Thus,

the LOAEL was considered to be 1.5 mg/kg/day for neurotoxic effects, and the NOAEL was accordingly established at 0.2 mg/kg/day. Application of an uncertainty factor of 3000 (10 for interspecies extrapolation, 10 for use of a subchronic study, 10 to protect sensitive individuals, and an additional 3 to account for lack of developmental data) to the NOAEL yielded an oral RfD of 7E-5 mg/kg/day.

Ellis, H.V., III, C.B. Hong, C.C. Lee, J.C. Dacre, J.P. Glennon. 1985. Subchronic and chronic toxicity studies of 2,4-dinitrotoluene. Part I. Beagle dogs. J. Am. Coll. Toxicol. 4:233-242.

Hong, C.B., H.V. Ellis, III, C.C. Lee, J.C. Dacre, J.P. Glennon. 1985. Subchronic and chronic toxicity studies of 2,4-dinitrotoluene. Part III. CD-1 mice. J. Am. Coll. Toxicol. 4:257-269.

Lee, C.C., C.B. Hong, H.V. Ellis, III, J.C. Dacre, J.P. Glennon. 1985. Subchronic and chronic studies of 2,4-dinitrotoluene. Part II. CD rats. J. Am. Coll. Toxicol. 4:243-256.

Endrin Ketone. Not available.

Heptachlor Epoxide. An oral RfD of 1.3E-5 mg/kg/day is verified and available on IRIS.

Methylene Chloride. An oral RfD of 6E-2 mg/kg/day is verified and available on IRIS.

4-Nitrophenol. An oral RfD is under review by the RfD Workgroup and is currently unavailable.

1,1,2,2-Tetrachloroethane. An oral RfD is under review by the RfD Work Group and is currently unavailable.

Trichloroethene. An oral RfD is currently under review by the RfD Work Group and. An interim oral RfD of 7E-3 mg/kg/day was derived in an Ambient Water Quality Criteria Document Addendum for Trichloroethylene (U.S. EPA, 1989).

U.S. EPA. 1989. Ambient Water Quality Criteria Document Addendum for Trichloroethylene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, Ohio, for the Office of Water Regulations and Standards.

Vinyl chloride. Not available.

B. ORAL SLOPE FACTORS

Acenaphthene. Not available. A cancer classification of D has been assigned to acenaphthene, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1990. Ambient Water Quality Criteria Document. Addendum for Acenaphthene. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Water Regulation and Standards.

Acetone. Verified as a Group D carcinogen on IRIS, thus data are inadequate for the derivation of a cancer slope factor.

Benzoic Acid. Verified as a Group D carcinogen on IRIS, thus data are inadequate for the derivation of a cancer slope factor.

Benzyl Alcohol. A cancer classification of E has been assigned (U.S. EPA, 1989). There is evidience of noncarcinogenicity in humans.

U.S. EPA 1989. Health and Environmental Effects Document for Benzyl alcohol. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response. Washington, D.C.

p-Bromodiphenyl Ether. Verified as a Group D carcinogen by the CRAVE Workgroup pending input onto IRIS. Therefore data are inadequate for the derivation of a slope factor.

Butanol. A cancer classification of D has been assigned thus data are inadequate for the derivation of a cancer slope factor (U.S. EPA, 1989).

U.S. EPA 1989. Health and Environment Effects Document for Butanol. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

Caprolactam. A cancer classification of E has been assigned to caprolactam. There is evidence of noncarcinogenicity in humans.

U.S. EPA 1988. Health and Environment Effects Document for Caprolactam. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

Carbon Disulfide. A cancer classification of D has been assigned

to carbon disulfide, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1986. Health and Environmental Effects Profile for Carbon disulfide. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response. Washington, D.C..

Chlorobenzene. Verified as a Group D carcinogen by the CRAVE Workgroup, pending input onto IRIS. Thus data are inadequate for the derivation of a slope factor.

Chloroethane. Not available. An interim oral slope factor is currently being developed by the Technical Support Center (TSC) and is expected to be available by the end of December.

Chloromethane. Classified as a Group C carcinogen with an oral slope factor of 1.3E-2 $(mg/kg/day)^{-1}$. This value is presented in HEAST.

U.S. EPA. 1987. Health Effects Assessment for Chloromethane. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, Ohio, for the Office of Emergency and Remedial Response, Washington, DC.

2-chlorophenol. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1989. Ambient Water Quality Criteria Document addendum for 2-chlorophenol. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Water Regulations and Standards.

1,3-dichlorobenzene. Verified as a Group D carcinogen by the CRAVE Workgroup, pending input onto IRIS.

Total 1,2-Dichloroethane. Verified as a Group B2 carcinogen on IRIS and HEAST with an oral slope factor or 9.1E-2 $(mg/kg/day)^{-1}$.

2,4-dichlorophenol. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA. 1989. Ambient Water Quality Criteria Document addendum for 2,4-Dichlorophenol. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste

and Emergency Response.

Diethylphthalate. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA. 1986. Drinking Water Criteria Document for Phthalic Acid Esters (PAEs). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Drinking Water.

2,4-dimethylphenol. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1990. Ambient Water Quality Criteria Document addendum for 2,4-dimethylphenol. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

Dimethylphthalate. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA. 1988. Drinking Water Criteria Document for Phthalic Acid Esters (PAEs). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Drinking Water.

Endosulfan. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1989. Ambient Water Quality Criteria Document for Endosulfan. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Water Regulation and Standards.

Endosulfan-Alpha and Beta. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1987. Health Effects Assessment for Endosulfan-Alpha and Beta. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

Ethylbenzene. Verified as a Group D carcinogen on IRIS, thus data are inadequate for the derivation of a cancer slope factor.

n-heptane. A cancer classification of D has been assigned, thus

data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1989. Health Environmental Effects Document for n-heptane. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

2-Hexanone. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S. EPA 1990. Health and Environmental Effects Document for 2-hexanone. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

N-Nitrosodiphenylamine. Verified as a Group B2 carcinogen and is on IRIS with an oral slope factor of 4.9E-3 $(mg/kg/day)^{-1}$.

Pentachlorophenol. Pentachlorophenol has been classified as a B2 carcinogen with an oral slope factor of 1.2E-1 per mg/kg/day. This assessment has been verified by the CRAVE Workgroup but is pending review by the Science Advisory Board. These verifications are based on both technical grade and Dowicide EC-7 NTP studies, pooled incidence of hepatocellular adenoma/carcinoma, pheochromocytoma/malignant pheochromocytoma, and hemangiosarcoma/hemangioma in female B6C3F1 mice. Quantitative estimates were reached by taking an average of the unit risks from the female mice exposed to technical grade and female mice exposed to Dowicide EC-7. The reasoning behind these estimates is that this gives extra weight to the hemangiosarcomas (using only the sex developing these tumors), recognizes other mechanisms, e.g., hepatotoxicity (by not using male mice with higher spontaneous rate), concurs with the 1986 Agency Guidelines in that three biologically relevant tumor types are pooled (rather than using only one tumor type), and accepts the Science Advisory Board's recommendation not to pool across sexes.

n-pentane. A cancer classification of D has been assigned, thus data are inadequate for the derivation of a cancer slope factor.

U.S.EPA 1987. Health Effects Assessment. Prepared by Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

Phenol. Verified as a Group D carcinogen by the CRAVE Workgroup, pending input onto IRIS.

Phthalic Anhydride. A cancer classification of E has been

assigned. There is evidence of noncarcinogenicity in humans.

U.S. EPA 1986. Health and Environmental Effects Document for Phthalic Anhydride. Prepared by Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Cincinnati, OH, for the Office of Solid Waste and Emergency Response.

Toluene. Verified as a Group D carcinogen on IRIS, thus data are inadequate for the derivation of a cancer slope factor.

1,2,4-Trichlorobenzene. Verified as a Group D carcinogen on IRIS, thus data are inadequate for the derivation on a cancer slope factor.

Trichlorofluoromethane. Not available.

1,1,1-Trichloroethane. Verified as a Group D carcinogen on IRIS, thus data are inadequate for the derivation of a cancer slope factor.

2,4,5-Trichlorophenol. Under review therefore not available at this time.

Total Xylenes. Verified as a Group D carcinogen on IRIS, therefore data are inadequate for the derivation of a cancer slope factor.

C. Status of Polyaromatic Hydrocarbons

I. RfD

A. Oral

Only 6 PAHs have interim oral RfDs. Table 1 lists the chemicals with oral RfDs along with the critical study, species, critical effect and reference dose. For the verified chemicals, the date of verification is listed; these chemicals are not currently loaded onto IRIS.

II. Carcinogenic Assessment

A. IRIS Status

Benzo(a)pyrene has been classified as a B2 carcinogen on IRIS, but a CRAVE-verified carcinogenic slope factor is not available because of lack of adequate data.

B. Interim Guidance

An oral slope factor of 11.5 $(mg/kg/day)^{-1}$ and an inhalation slope factor of 6.1 $(mg/kg/day)^{-1}$, calculated for benzo(a)pyrene in the Health Effects Assessment for PAHs (EPA, 1984), can be adopted as interim numbers pending verification by the Work Group.

The classification for fourteen PAHs were discussed and verified at CRAVE Work Group Meetings. (Fluoranthene and phenanthrene were verified in May, 1990. The remaining 12 PAHs were verified in February, 1990.) Interim carcinogenic classifications are listed below:

Acenaphthylene - D
Anthracene - D
Benz(a)anthracene - B2
Benzo(b)fluoranthene - B2
Benzo(k)fluoranthene - B2
Benzo(g,h,i)perylene - D
Chrysene - B2
Dibenz(a,h)anthracene - B2
Fluoranthene - D
Fluorene - D
Indeno(1,2,3-c,d)pyrene - B2
Naphthalene - D
Phenanthrene - D
Pyrene - D

References

NTP (National Toxicology Program). 1980. Unpublished subchronic toxicity study: Naphthalene (C52904), Fischer 344 rats. Prepared by Battelle's Columbus Laboratories under Subcontract No. 76-34-106002. March.

U.S. EPA. 1988. 13-week mouse oral subchronic toxicity study. Prepared by Toxicity Research Laboratories, LTD., Muskegon, MI for the Office of Solid Waste, Washington, DC.

U.S. EPA. 1989a. Mouse oral subchronic study with acenapthene. Study conducted by Hazelton Laboratories, Inc., for the Office of Solid Waste, Washington, DC.

U.S. EPA. 1989b. Subchronic toxicity study in mice with anthracene. Conducted by Hazelton Laboratories, Inc., for the Office of Solid Waste, Washington, DC.

U.S. EPA. 1989c. 13-week mouse oral subchronic toxicity study. Prepared by Toxicity Research Laboratories, LTD., Muskegon, MI for Office of Solid Waste, Washington, DC.

U.S. EPA. 1989d. Mouse oral subchronic toxicity with pyrene. Study conducted by Toxicity Research Laboratories, LTD., Muskegon, MI for the Office of Solid, Washington, DC.

TABLE 1

Oral RfDs for PAHs

Compound/ Status	Exposure	Species	Critical Effect	Uncertainty Factor	Modifying Factor	Reference Dose	Reference
Acenapthene / Verified (11/15/89)							
	175 mg/kg/day daily by gavage for 90 days (NOAEL); 350 mg/kg/day (LOAEL)	Mouse	Hepatotoxicity	3000	1	6E-2 mg/kg/day	U.S. EPA, 1989a
Anthracene / Verified (11/15/89)							
	1000 mg/kg/day daily by gavage for 90 days (NOEL)(HDT)	Mouse	No effects	3000	1	3E-1 mg/kg/day	U.S. EPA, 1989b
Fluoranthene / Verified (11/15/89)							
	125 mg/kg/day daily by gavage via corn oil for 13 weeks (NOAEL); 250 mg/kg/day (LOAEL)	Mouse	Nephropathy, increased relative liver weights, hematological and clinical effects	3000	1	4E-2 mg/kg/day	U.S. EPA, 1988
Fluorene / Verified (11/15/89)							
	Gavaged via corn oil 125 mg/kg/day for 13 weeks (NOAEL); 250 mg/kg/day (LOAEL)	Mouse	Decreased RBC, packed cell volume and hemoglobin	3000	1	4E-2 mg/kg/day	U.S. EPA, 1989c
Napthalene							
	50 mg/kg/day in diet for 5 days/week for 13 weeks (35.7 mg/kg/day)	Rat	Decreased body weight gain.	10,000	1	4E-3 mg/kg/day	NTP study (1980)

TABLE 1 (cont.)

Oral RfDs for PAHs

Compound/ Status	Exposure	Species	Critical Effect	Uncertainty Factor	Modifying Factor	Reference Dose	Reference
Pyrene / Verified (11/15/89)							
	75 mg/kg/day by gavage via corn oil for 13 weeks (NOAEL)	Mouse	Nephropathy and decreased kidney weight	3000	1	3E-2 mg/kg/day	U.S. EPA, 1989d

HDT = Highest Dose Tested